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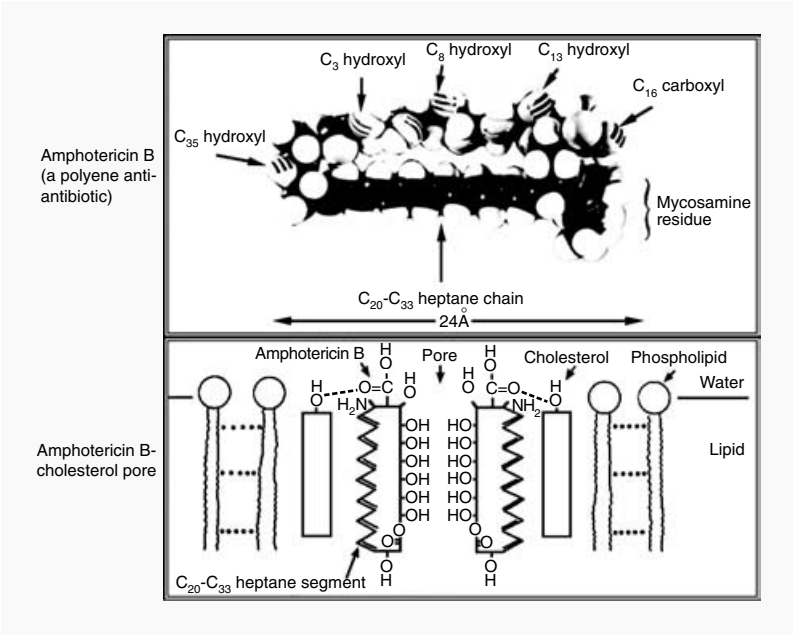
The amphotericin B–cholesterol pore model



We know from transport studies in planar lipid bilayer membranes (*J Gen Physiol* 52:300, 1968; *J Gen Physiol* 53:133, 1969) that nystatin and amphotericin B produce functional pores in the bilayers, but only when the latter contains cholesterol. The model shown above for an amphotericin B–cholesterol pore (*Kidney Int* 4:337, 1973) depended on the following considerations: Corey-Pauling space filling models of cholesterol were rod-like, with hydrophilic 3β-hydroxyls at one end of an otherwise hydrophobic molecule spanning approximately 20 Å. Corey-Pauling space-filling models of amphotericin B, also 24-Å long, contained highly hydrophilic mycosamine residues attached to two hydrocarbon tails, a hydrophilic chain containing multiple hydroxyl groups, and, in parallel, a hydrophobic heptane chain. The two chains were linked at the end of the molecule by yet another hydroxyl group. Thus, amphotericin B resembles a counterfeit phospholipid.

We therefore considered that the amphotericin B–cholesterol pore had the configuration shown above, with hydrophilic hydroxyl groups lining the pore, or channel, and the hydrophobic heptane segments interacting with cholesterol and the hydrophobic interior of the bilayer. Furthermore, following the arrangement shown above, it was possible to construct a cylindrical structure about 6 to 7 Å in radius lined with hydroxyl groups and covered with alternating heptane chains and sterol nuclei. Thus, the amphotericin B–cholesterol pore served as an early model for pores, or channels, in biologic membranes.